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### REMARKS

Claims 25 has been cancelled without prejudice, and claims 26-30 have been added. No new matter has been added by virtue of the new claims. For instance, support for the new claims appears e.g. at pages 7-8 and the original claims of the application.

Claims 12-24 were rejected under 35 U.S.C. 112, first paragraph.

As grounds for the rejection, it is stated that the only working example of an A group is a particular group and "[t]herefore, a persons of skill in the art would deem that Applicant did not possess the entire invention as claimed at the time of the filing."

It is also stated that "the specification, while being enabling for treating some cancers, does not reasonably provide enablement for treating all cancers."

The rejection is traversed.

As discussed in Applicants' prior response, the present application fully satisfies the rejection of 35 U.S.C. 112, including the make and use requirements of Section 112, first paragraph.

Thus, as discussed in Applicants' prior response, compounds of Formula I are disclosed at pages 1 through 2 of the application, with detailed elaboration of those compounds set forth at 3 through 10 of the application. An extensive number of synthesis examples are also set forth in the application as filed.

Clearly based on such extensive disclosure as the present application, the skilled worker would have been able to make compounds of the invention.

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Therapeutic uses of compounds of are detailed for instance at pages 9 through 12 of the application.

Applicants also again point out that no substantiating reasons have been advanced as to why one skilled in the art could not make and use the claimed invention. Indeed, the discussion above makes clear that one skilled in the art could readily practice the claimed invention in view of Applicants' disclosure.

Respectfully, such a rejection, lacking any supporting evidence or other substantiating grounds is simply not proper. Thus, for example, MPEP §2164.04 states the following (quoting *In re Marzocchi*, 169 USPQ 367):

[I]t is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure.

In view thereof, withdrawal of the rejection is requested.

Applicants also are submitting under separate cover a Rule 132 Declaration which details biological data of the present compounds.

Claims 12-23 were rejected under 35 U.S.C. 103 over Nicolaou et al. (*Angew Chem. Int. Ed.* 1998, 2014-2045) in view of Patani et al. (*Chem. Rev.* 1996, 3176).

It has been acknowledged that "Niocolau et al. do not teach a thioether or a SO<sub>2</sub> in place of the carbonyl next to the gem-dimethyl of the epothilone ring."

Nevertheless, the position has been taken that Patani reports "that carbonyl can be replaced by S, SO, SO<sub>2</sub> if the position is not essential to the function of the molecule."

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The rejection is traversed.

As discussed in Applicants' prior response, Patani is merely a background article and provides no motivation sufficient to sustain the instant Section 103 rejection to modify the Nicolaou et al. document as has been proposed.

Indeed, the structural distinction between Applicants' claimed compounds and the compounds of the Nicolaou et al. document (such distinctions specifically acknowledged in the Office Action) makes clear that a *prima facie* case under Section 103 does not exist here.

For example, as discussed in the prior response, in *In re Grabiak*, 226 USPQ 872, the Court of Appeals for the Federal Circuit reversed a rejection under Section 103 on the basis that the cited document provided no suggestion to replace oxygen (in the ester of the cited document) with sulfur (to provide the thioester of the claimed compound). The Federal Circuit particularly noted (page 872):

The PTO cited no pertinent reference showing or suggesting to one of ordinary skill in the art the change of the thioester for an ester group. In the absence of such reference, there is inadequate support for the PTO's position that this modification would *prima facie* have been obvious.

In view thereof, reconsideration and withdrawal of the rejection is requested.

Applicants also are submitting under separate cover a Rule 132 Declaration which further confirms the patentability of the present compounds.

Claims 12-23 and 25 were provisionally rejected on grounds of obviousness-type double patenting over certain claims of U.S. application no. 10/520769 in view of Patani et al. The rejection is traversed.

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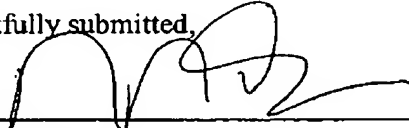
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As discussed above, Patani et al. is merely a background document and provides no suggestion to modify the cited copending application claims in a manner sufficient to sustain the instant rejection.

Moreover, this provisional rejection can be properly withdrawn if it is the only outstanding rejection in the case. See Section 804 of the Manual of Patenting Examining Procedure.

Accordingly, withdrawal of the rejection is requested.

Respectfully submitted,



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